REMARKS

Any fees that may be due in connection with this application throughout its pendency may be charged to Deposit Account No. 50-1213.

Claims 125-130 are cancelled. Claims 1-124 and 131-143 are pending. Claims 15, 68, 131 and 134 are amended.

Claim 15 is amended to replace the chemical compound name "hepatoporphyrin" with the chemical compound name " hematoporphyrin". The amendment finds basis on page 26, line 3, which discusses the compound "hematoporphyrin".

Claim 68 is amended to correct a claim dependency error. Claim 9 provides proper antecedent basis for the mixture discussed in claim 68. Hence, claim 68 is amended to depend on claim 9.

Claims 131 and 134 are amended to correct improper claim dependencies. Claim 109 provides the antecedent basis for the method of photodynamic therapy, first introduced in the independent claim 30, comprising illuminating the treatment area. Hence, claims 131 and 134, which further expand upon the act of illuminating, first introduced in claim 109, have been amended to depend on claim 109.

New claims 137-143 are added and basis can be found in the application as originally filed. For example claim 137 finds basis in claim 28 and in the specification at paragraph on page 3, lines 12-20. Claims 138-143 find basis in the claims 125-136 as originally filed.

Specification is amended to correct obvious typographical, spelling and formatting errors.

No new matter has been added.

Included as an attachment is a marked-up version of the specification paragraphs and claims, per 37 CFR §1.121.

* * *

Entry of this amendment and examination of the application are respectfully requested.

Respectfully submitted,
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: JAMES CHEN
Serial No.: 10/091,144
Filed: March 4, 2002

For: *NOVEL USES OF PHOTOLUMINESCENT NONOPARTICLES FOR PHOTODYNAMIC THERAPY*

Art Unit: 1615
Examiner: Unassigned

ATTACHMENT TO THE PRELIMINARY AMENDMENT
MARKED UP PARAGRAPHS AND CLAIMS (37 CFR §1.121)

IN THE SPECIFICATION:

Please amend the specification as follows:

Please amend the paragraph on page 1, lines 17-28, as follows:

PDT is a form of energy-activated therapy for destroying abnormal or diseased tissue. The procedure for this treatment includes administration of a photosensitive [compounds] compound (a PDT drug) to a [patent] patient, followed by illumination with light having a wavelength or waveband corresponding to a characteristic absorption wavelength of the photosensitive compound. Upon illumination, the photosensitive compound absorbs photons from the light source and transfers this energy to surrounding oxygen molecules. This in turn induces formation of singlet oxygen and other highly-reactive free radical species, leading to a number of biological effects, including damages to proteins, nucleic acids, lipids, and other cellular components, and often ultimately results in cell death.

Please amend the paragraph on page 2, line 1-12 as follows:

PDT drugs may be administered to a patient by ingestion or injection or by applying the compound to a specific treatment site on the [patent's] patient's body. These compounds characteristically accumulate at higher concentrations in rapidly-growing tissue, such as malignant tumors, than in normal tissue.

Typically, after administering a PDT drug intravenously and then waiting a period of time, the drug clears from normal tissues and is preferentially retained by rapidly-growing tissues. The drug remains inactive until exposed to light. Application of light of a suitable wavelength photoactivates the drug, resulting in generation of reactive species and damage to neighboring tissue. PDT has been used to treat various types of malignant tumors as well as non-cancerous [condition] conditions such as macular degeneration and atherosclerosis.

Please amend the paragraph on page 2, lines 13-29, as follows:

Light sources utilized for PDT include monochromatic lasers linked to fiber optics and light emitting diode (LED) arrays. One disadvantage of such light sources is that they are not capable of broadband emission at multiple wavelengths or wavebands at which a drug can be activated. Often a PDT drug can be activated at more than one wavelength. To obtain light of multiple wavelengths, light from multiple lasers and/or from multiple LEDs must be coupled into a fiber optic. Lasers can be bulky, requiring in-office or in-hospital administration of light and requiring a significant amount of valuable space to house the multiple lasers. Further LEDs may not provide all wavelengths desired. The technology to provide LEDs producing blue, violet, and ultraviolet light is developing, but LEDs are not yet available to provide the full spectrum of specific wavelengths that can be useful to [active] activate PDT drugs. Further, light in a waveband from the blue to ultraviolet part of the spectrum does not penetrate tissue very deeply. Consequently, any light administered via laser or LED array in this portion of the spectrum only penetrates shallow portions of tissue at the site where light is introduced to the body.

Please amend the paragraph on page 3, lines 12-20, as follows:

The invention in one embodiment provides a photodynamic therapy in which light-emitting nanoparticles are administered to a patient in addition to a PDT drug in order to activate the drug. The light-emitting nanoparticles absorb light from the light source and re-emit light at a different wavelength, one which is suitable to activate the PDT drug in the vicinity of the light emitting

nanoparticles. The PDT drug near the light-emitting nanoparticles is activated, thus treating the disease any place that the PDT drug and nanoparticles are located and that light from the light [from the light] source can reach.

Please amend the paragraph on page 9, lines 6-12, as follows:

Quantum dots are small molecular clusters having up to about a few hundred atoms. Quantum dots are therefore larger than individual atoms, but quantum dots generally behave in accord with the principles of quantum mechanics that govern the behavior of individual atoms. Because of this behavior, quantum dots are sometimes also called "artificial atoms." Quantum dots have a size in the [regime] region of about 1 nm to about 20 nm and are typically only a few nanometers in size.

Please amend the paragraph on page 9, lines 13-27, as follows:

A quantum dot is typically composed of a semiconductor material or materials, metal(s), or metal oxides exhibiting a certain bandgap energy. Although it is preferred that biocompatible light-emitting nanoparticles such as TiO_2 are used in the practice of the invention, nanoparticles that are not generally considered to be biocompatible may also be used. A variety of materials may be utilized for construction of nanoparticles, including but not limited to TiO_2, Al_2O_3, AgBr, CdSe, CdS, CdS_xSe_{1-x}, [CuC1] CuCl, $CdTe_xS_{1-x}$, ZnTe, ZnSe, ZnS, GaN, InGaN, InP, CdS/HgS/CdS, and InAs/GaAs. Group II-VI, Groups III-V, and Groups I-VII semiconductors as well as Group IV metals and alloys from quantum dots and other nanoparticles as described below when formed sufficiently small. A quantum dot may also be surrounded by a material or materials having wider bandgap energies (for example, ZnS-capped CdS), and especially may be surrounded by those materials that improve biocompatibility of the nanoparticles.

Please amend the paragraph on page 33, line 18, through the paragraph on page 34, line 2, as follows:

The activating light source emits light that the nanoparticles absorb. Consequently, if all the nanoparticles [all] absorb light at about the same

wavelength, a narrow-band light source such as a laser can be used. Or, if the nanoparticles absorb light at different wavelengths, a broader-band light source may be used such an LED array. Light-emitting nanoparticles may themselves be a light source for other light-emitting nanoparticles as described previously in order to allow a light source to be used that produces light of a wavelength that is absorbed by some of the nanoparticles but not all of them. In this case, the nanoparticles acting as a light source for other nanoparticles absorb the actinic radiation from the light source, then emit radiation at a second wavelength that at least some of the other nanoparticles absorb, causing them to fluoresce. In another preferred embodiment of the invention, a narrow-band light source such as a laser is used to activate a mixture of nanoparticles whose emission provides a broad band of light.

IN CLAIMS:

Please amend claims 15, 68, 131 and 134 as follows:

15. (Amended) A method according to claim 14, wherein the photosensitive compound is selected from the group consisting of indocyanine green; methylene blue; toluidine blue; aminolevulinic acid; phthalocyanines; porphyrins; texaphyrins; bacteriochlorins; merocyanines; psoralens; benzoporphyrin derivatives; porfimer sodium and its pro-drugs; *a*-aminolevulinic acid; protoporphyrin; chlorin compounds; purpurins; mono-, di-, or polyamide aminodicarboxylic acid derivatives of cyclic or non-cyclic tetrapyrroles; alkyl ether derivatives of pyropheophorbide-a with N-substituted cyclic imides; derivatives of mono-L-aspartyl chlorin e6 (NPe6); pheophorbides and pyropheophorbides; porfimer sodium; omeprazole; benzoporphyrin verteporfin; [hepatoporphyrin] <u>hematoporphyrin</u> derivatives; and dihematoporphyrin ether.

68. A mixture according to claim [69] <u>9,</u> wherein said first wavelength and said third wavelength are equal.

131. A method according to claim [30] <u>109,</u> wherein the act of illuminating the treatment area with light from said light source that emits said

131. A method according to claim [30] 109, wherein the act of illuminating the treatment area with light from said light source that emits said light of said second wavelength, thereby causing the light-emitting nanoparticles to emit said light of the first wavelength, comprises: illuminating a total internal reflection lens with said light from the light source and illuminating the nanoparticles with light transmitted by the total internal reflection lens.

134. A method according to claim [30] 109, wherein the act of illuminating the treatment area with light from said light source that emits said light of said second wavelength, thereby causing the light-emitting nanoparticles to emit said light of the first wavelength, comprises: illuminating a total internal reflection lens with the light of the first wavelength generated by the nanoparticles, and illuminating the treatment area with light transmitted by the total internal reflection lens.